and are discussed in detail below. Claims 1, 2, and 8 have been amended to correct an obvious typographical error. Claims 1 and 2 have been amended for clarity and support is found both implicitly and explicitly within the specification; see for example page 16, lines 1-2; page 4, lines 4-5; in original claim 21. Claim 8 has been further amended for clarity and support is found at page 34, line 1 to page 36, line 4. New Claims 27-42 have been added. Support for Claim 27 is found at page 31, line 22 to page 32, line 15;
Claims 28-30 at page 12, lines 3-7; and Claims 31-42 at page 16, line 15 to page 23, line 28.

New matter has not been introduced by way of amendment. Favorable consideration of the following comments relative to the outstanding rejections as they may apply to the present claims is respectfully requested for the reasons that follow.

The specification has been amended to comply with the sequence disclosure requirements (*see* attached copy of Notice to Comply). This amendment is accompanied by a floppy disc containing the above named sequences, SEQUENCE ID NUMBERS 1-33, in computer readable form, and a paper copy of the sequence information. The computer readable sequence listing was prepared through use of the software program "PatentIn" provided by the PTO. The information contained in the computer readable disc is identical to that of the paper copy. This sequence listing and amendment to the specification contains no new matter. Applicants submit that this amendment, the accompanying computer readable sequence listing, and the paper copy thereof serve to place this application in condition of adherence to the rules 37 C.F.R. § 1.821-1.825.

Claim 8 stands rejected under 35 U.S.C. §112, second paragraph for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. The Examiner contends Claim 8 is indefinite in reciting "an exogenous precursor" because the product of the precursor is not unambiguously defined. Applicants traverse the rejection.

"Precursors" is defined at page 34, line 1 to page 36, line 4 as compounds that are altered by the disclosed enzyme complexes to form bioactive agents. "Bioactive agents" is defined at page 34, lines 3-6 as "any molecule...with the capability of directly or indirectly altering a cellular phenotype." In view of these definitions,

Applicants assert that a precursor-product relationship is defined in the specification. Nevertheless, to expedite prosecution, Claim 8 has been amended to recite "bioactive agent precursor".

In view of these remarks and amendments, Applicants respectfully assert that the requirements set forth in §112, second paragraph have been fulfilled and respectfully request the Examiner to withdraw the rejection.

Claims 1-8 stand rejected under 35 U.S.C. §102(e) as being anticipated by Khosla *et al.* (U.S. Patent No.: 5,672,491). Khosla *et al.* discloses cells transformed with polyketide synthase gene clusters that encode and express 6-deoxyerythronolide B synthase (DEBS), a multifunctional protein consisting of three polypeptides. The Examiner contends that the three DEBS polypeptides bind or interact with each other to form DEBS and, therefore, one of the three DEBS polypeptides functions as a scaffold with respect to the other two polypeptides. Applicants traverse the rejection.

To underscore a fundamental difference between the claimed scaffold and the disclosure of Khosla *et al.*, the claims have been amended to state that the claimed exogenous scaffold has no enzymatic activity; the scaffolds are not biologically reactive. In contrast, each of the three DEBS polypeptides disclosed by Khosla *et al.* possess enzymatic activity (*see* Column 15, lines 1-7 and 19-20). Therefore, if a DEBS polypeptide is construed as being a scaffold relative to the other DEBS polypeptides, it would also possess enzymatic activity. In view of this difference between Khosla *et al.* and the claimed invention, Khosla *et al.* do not teach expicitly or impliedly every element of the claimed invention and do anticipate under §102(e).

In view of these remarks and amendments, Applicants respectfully request the Examiner to withdraw the rejection.

Claims 1-8 stand rejected under 35 U.S.C. §103(a) as being obvious in view of Bott *et al.* (WO 97/14789). The Examiner contends that the catalytic array of Bott *et al.* comprising one or several enzymes bound to a scaffoldin protein, and a host cell transformed with expression vectors encoding either the scaffoldin protein or one or more enzymes establish a *prima facie* case of obviousness. Despite the Examiner's acknowledgment that Bott *et al.* do not disclose a host cell transformed with expression vectors encoding a scaffoldin protein and two or more enzymes (*see* Claims 1 and 2),

the Examiner contends that a cell so transformed would have been obvious to one or ordinary skill in the art. Applicants traverse the rejection.

As outlined in the M.P.E.P. §2143, to establish a *prima facie* case of obviousness, three basic criteria must be met: i) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; ii) there must be a reasonable expectation of success; and iii) the prior art reference (or references when combined) must teach or suggest all the claim limitations.

To provide a suggestion or motivation to modify the reference, the prior art must suggest the desirability of the claimed invention (M.P.E.P. §2143.01). The invention as defined in Claims 1 and 2, respectively, is directed to: i) cells comprising an exogenous scaffold having no enzymatic activity and comprising first and second binding sites; and at least two enzymes, one of which is heterologous to the cell, that are capable of binding to the scaffold and ii) cells comprising a nucleic acid encoding a exogenous scaffold and a nucleic acid encoding two enzymes.

> The host cells of Bott *et al.* are defined at page 7, lines 8-10:
> "Host strain" or "host cell" means a suitable host for an expression vector comprising DNA encoding the scaffoldin protein or (emphasis added) the enzyme-dockerin protein according to the present invention.

From this definition it can be concluded that host cells as defined by Bott *et al.* express either a scaffoldin protein or the enzyme protein. The scaffolds of Bott *et al.* are defined at page 6, lines 6-10, as "a peptide backbone found in cellulosomal or amylosomal complexes." Examples include the CipA, CipB, and CbpA proteins. The enzyme arrays are assembled extracellularly using scaffold and enzyme that are individually expressed and purified from recombinant bacterial cells (*see* page 19, lines 10-36).

Bott *et al.* are silent with respect to the cells comprising both a scaffold and at least two enzymes and cells comprising nucleic acids that encode a scaffold and at least two enzymes. According to the requirements concerning "desirability" as outlined in the M.P.E.P. §2143.01, Bott *et al.* do not suggest the desirability of the claimed cells comprising enzymatic arrays. In fact, all the uses outlined in Bott for the enzymatic complexes require extracellular complexes: the abstract suggests the use of the

complexes in "recovery systems, targeted multi-enzyme delivery systems, soluble substrate modification, quantification type assays, and other applications in the food industry, feed, textiles, bioconversion, pulp and paper production, plant protection and pest control, wood preservatives, topical lotions and biomass conversions". See also page 8, lines 25-29: the complexes may comprise "a cellulase and a xylanase for use in hydrolyzing lignocellulosic material or a combination of a protease, an amylase, a cellulase and a lipase for use in detergents". All of these utilities are directed to extracellular applications; that is, one could not efficiently digest lignin if the enzymes are within a cell, since this would require the transport of the lignin into the cell.

Furthermore, the differences between Bott *et al.* and the claimed subject matter described above demonstrate that Bott *et al.* do not teach or suggest all the claim limitations.

In view of these remarks, Applicants respectfully assert that the Bott *et al.* reference does not fulfill the three basic requirements for establishing a legal conclusion of obviousness and, therefore, Applicants respectfully request the Examiner to withdraw the rejection.

CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 781-1989.

Respectfully submitted,

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